

# EXHIBIT 105

## Alzheimers and Investing < <https://ad-science.org/>>

Just research. Not financial advice

Oct 21 2021 < <https://ad-science.org/2021/10/21/notes-from-a-molecular-biologist/>>

# Notes from a Molecular Biologist

*The author of this post received a Ph.D. degree in Molecular Biology and has been an academic researcher since 2003. His laboratory studies cancer and other human diseases and routinely run western blots (~1,000/year) for their studies.*

I thought it might be helpful to post an expert's review of the concerns raised in the Labaton Sucharow Citizen Petition (CP) regarding western blot (WB) data for Cassava Science's Alzheimer's drug. Simufilam has demonstrated remarkable improvement in cognition in Alzheimer's patients at 12 months of treatment in an open label study and the drug is entering two pivotal phase III studies.

Western blotting is a research tool that we use to analyze proteins, including their levels, modifications, and association with other proteins. Protein extracts are prepared from cells or tissue, denatured using a detergent and heating, and then loaded onto a gel, which is a matrix of polyacrylamide, and then a current applied. This allows for proteins to be separated based on their size (i.e. molecular weight (MW)). After the gel is "run", the proteins are transferred (i.e. blotted) onto a membrane and then probed with an antibody specific for whatever protein you want to analyze. The blot is then probed again, this time with a secondary antibody that is enzyme-linked and binds to the first antibody, thus allowing for detection using a chemiluminescent reagent that produces light where the first antibody binds the membrane (thus producing what is known as a "band"). All WBs include analysis of a control protein (e.g. actin, GAPDH) to confirm that equal amounts of protein extract were loaded in each lane.

The first thing to understand about WBs is that they are semi-quantitative. They can basically tell you if there are differences in levels (increases, decreases) or presence of a modification or binding protein. Secondly, the western blotting technique is somewhat of an artform. It takes practice knowing what procedures are best to analyze a specific protein. Thirdly, there are a lot of variables. Researchers use different first and second antibodies, gel conditions, membrane supports, washing and exposing conditions. There is no standardized protocol. For example, many academic labs that are on a budget will pour their own gels as opposed to buying more expensive pre-made gels. With the former, you have more control over your analysis, but the WBs can often look a little dirtier, lanes slightly unevenly spaced, or bands looking not so sharp.

My overall impression of the CP is that it does exactly what it set out to do- confuse the average investor and seed doubt so that they sell their shares. The average investor has no idea what a WB is let alone how to objectively analyze them. The majority of concerns raised are easily explained and a small number of others are obvious errors that likely occurred during generating figures for publication. There is no obvious evidence of systematic data manipulation or scientific misconduct. Someone with knowledge of molecular biology likely helped put together the CP, but many of the concerns raised show a shallow understanding of WB technique and data analysis. Below, I provide responses to general concerns and then a point-by-point analysis of each concern raised in the CP.

General concerns raised in the petition:

1. It is stated that “the western blot data presented by Wang/Burns are almost always overexposed and highly processed, which has been repeatedly seen in previously reported examples of image manipulation.” Several of the studies scrutinized in the CP were published between 2005-2012. It is important to realize that during this time WBs were visualized by exposing the membrane to film. Control proteins generally give very strong signals due to their high level of expression in cells and use of validated antibodies that give the best (i.e. strongest) signal. Also, analysis of low-expressed proteins requires more extract to be run per lane to see the signal. These factors can often lead to control bands that are strong (i.e. overexposed). Today, most researchers use digital imaging systems to expose WBs, which avoids issues with overexposure. As far as the claim of “highly processed” images, know that most research papers published pre-2010 used images of 300-600 dpi or lower. Images retrieved from online papers, as was done for the CP, are likely even lower resolution. In my opinion, it is dangerous to take a low-resolution WB and adjust the contrast and brightness levels to attempt to uncover evidence of data manipulation. For example, the CP repeatedly shows changes in background pixels as evidence of data manipulation, but there are many factors that could give this effect. Over the years, I’ve seen things as simple as streaks on a film caused by the processor or how the membrane is wrapped with layers of plastic wrap to prevent drying from influencing the background of the figure.
2. It is repeatedly said in the CP that the authors should produce the original WB data in order to satisfy their concerns. I’m pretty sure the scientists behind the CP know that this request is unreasonable. Most researchers will store data after publication in case questions do arise. In a perfect world, films and electronic WB data would be stored forever, but students leave the lab, labs downsize or move to new institutes, and thumb drives get lost. In addition, journals generally don’t require researchers to keep data for longer than a year or so. The fact that Drs. Wang/Burns have not “answered” the WB concerns of the CP is likely not due to them hiding something but rather that it is impossible to retrieve data used in a publication 10-15 years ago. Journals rely on a thorough analysis of the data by the reviewers, which are generally 3 experts in the field. If a reviewer had a problem with any of the WBs in question, they could have asked for them to be repeated. If they thought the data were manipulated in any way, the reviewers would have instantly rejected the paper and likely notified the journal.

3. The CP repeatedly says that their analysis indicates fraud or scientific misconduct. Scientific misconduct is a very serious claim. As scientists, we welcome critiques of our data presented in research papers or presentations. That is part of being a scientist. But know that scientists are trained from early in their careers and throughout about what constitutes misconduct. We take refresher courses and sign statements when we submit research papers regarding the validity of our work. Every researcher knows that being accused of misconduct can instantly ruin a career. In my years as an academic researcher, I have never known of anyone who was even accused of scientific misconduct. I'm not saying that it doesn't happen, but there is a big difference between a paper mill in China that is duplicating figures in different publications and an established researcher whose lab has consistently published quality papers and is supported by NIH funding. It is improbable to think that Drs. Wang/Burns have systematically produced fraudulent research and manipulated data for research publications and grant applications without a colleague, collaborator, or reviewer detecting it for 15+ years.

In the next article, I will follow up on specific allegations made in the petition.

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## 12 Comments

 Travis S

**October 21, 2021 at 5:01 pm < <https://ad-science.org/2021/10/21/notes-from-a-molecular-biologist/#comment-45>>**

Beautiful read. But, would be nice to see the actual people who wrote it and their credentials. I feel this article would have much more weight with that. Otherwise, good read.

★<[https://ad-science.org/2021/10/21/notes-from-a-molecular-biologist/?like\\_comment=45&\\_wpnonce=3491901d9c](https://ad-science.org/2021/10/21/notes-from-a-molecular-biologist/?like_comment=45&_wpnonce=3491901d9c)>

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 Aang

Its hard for credible scientists to reveal their names and not risk harassing emails. All i can tell you is that no amateur could write this article. Thank you for your comments.

★< [https://ad-science.org/2021/10/21/notes-from-a-molecular-biologist/?like\\_comment=46&\\_wpnonce=0d01c5ba89](https://ad-science.org/2021/10/21/notes-from-a-molecular-biologist/?like_comment=46&_wpnonce=0d01c5ba89)>

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 cotdt

**October 22, 2021 at 9:07 pm < <https://ad-science.org/2021/10/21/notes-from-a-molecular-biologist/#comment-56>>**

If you look at Part 2, it is explained in such detail that one can judge for themselves the credibility:

<https://ad-science.org/2021/10/21/of-shorts-and-bLOTS/> <<https://ad-science.org/2021/10/21/of-shorts-and-bLOTS/>>

★< [https://ad-science.org/2021/10/21/notes-from-a-molecular-biologist/?like\\_comment=56&\\_wpnonce=0d973fdec6](https://ad-science.org/2021/10/21/notes-from-a-molecular-biologist/?like_comment=56&_wpnonce=0d973fdec6)>

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 Terence Farrell

**October 21, 2021 at 7:45 pm < <https://ad-science.org/2021/10/21/notes-from-a-molecular-biologist/#comment-47>>**

Thank you for sharing your thoughts and analysis. Lay people and SAVA investors know in the back of their mind that the claims in the CP are blatant misrepresentations generated to undermine the stock price and company. However they don't have the knowledge or credentials to stand up and refute them as you have done. It is important and beneficial, and it's appreciated.....



Alberto <<https://www.inmodelarosa.com>>

**October 22, 2021 at 2:55 am <<https://ad-science.org/2021/10/21/notes-from-a-molecular-biologist/#comment-48>>**

Un buen artículo y sin duda muy aclaratorio.

★<<https://ad-science.org/2021/10/21/notes-from-a-molecular-biologist/>>

like\_comment=48&\_wpnonce=af5fef0025>

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replytocom=48#respond>

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Gary M

**October 22, 2021 at 5:51 am <<https://ad-science.org/2021/10/21/notes-from-a-molecular-biologist/#comment-49>>**

Thank you for taking the time to write such a detailed and informative article. Clearly written by a subject matter expert. For transparency I think you should disclose whether you own any SAVA or not. I look forward to your next article.

★<<https://ad-science.org/2021/10/21/notes-from-a-molecular-biologist/>>

like\_comment=49&\_wpnonce=49749b8399>

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replytocom=49#respond>

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Retired MD, PhD

**October 22, 2021 at 6:48 am <<https://ad-science.org/2021/10/21/notes-from-a-molecular-biologist/#comment-50>>**

This all fine and actually meaningless on both sides of the isle. The real issue is Wangs ultimate work on pTau and amyloid monomers analysis/quantitation was independently reconfirmed by Quanterix. Thus, two independent labs, using different methodologies and different samples (plasma vs cerebrospinal fluid) confirmed each other. It does not get any more credible than that.

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★<[https://ad-science.org/2021/10/21/notes-from-a-molecular-biologist/?like\\_comment=50&\\_wpnonce=a786b38d1b](https://ad-science.org/2021/10/21/notes-from-a-molecular-biologist/?like_comment=50&_wpnonce=a786b38d1b)>

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Super DD

October 22, 2021 at 7:46 am <<https://ad-science.org/2021/10/21/notes-from-a-molecular-biologist/#comment-52>>

I don't have a science background, and am long with SAVA. It would be idea if this Ph.D could have a direct dialog with Dr. Bik or someone in the science field could confront Dr. Bik with findings and comments of this Ph.D on PubPeer.

This is what I have found by searching for all Dr. Wang's publications on

<https://pubpeer.com/search?q=Hoau-Yan+Wang> <<https://pubpeer.com/search?q=Hoau-Yan+Wang>>

Out of 22 Dr. Wang's papers which have received questions on PubPeer, 7 were published later than 2012, while other 15 were before 2012. And Dr. Bik has expressed her doubts on 2 of those 7, with a most recent comment on Oct 2021:

1. Prenatal cocaine exposure uncouples mGluR1 from Homer1 and Gq Proteins PLoS ONE (2014)
2. PTI-125 binds and reverses an altered conformation of filamin A to reduce Alzheimer's disease pathogenesis  
Neurobiology of Aging (2017)

Many thanks,  
Super DD

★<[https://ad-science.org/2021/10/21/notes-from-a-molecular-biologist/?like\\_comment=52&\\_wpnonce=35d33df6d6](https://ad-science.org/2021/10/21/notes-from-a-molecular-biologist/?like_comment=52&_wpnonce=35d33df6d6)>

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cotdt

**October 22, 2021 at 9:19 pm < <https://ad-science.org/2021/10/21/notes-from-a-molecular-biologist/#comment-57>>**

I'm not the author of this article but I've looked at many of these fraud accusations and they are along the same lines of editing artifacts. So, the lab's undergrad used editing to clean up the graphics to make the paper look cleaner. This is probably not a good practice precisely because of this situation. But why does one have to accuse Dr. Wang of fraud and spread this information all over the internet, in an attempt to crucify Dr. Wang? Just to drive down the stock price? What a shame it is to be a FUD spreader. If I see errors in Dr. Bik's papers, I would have the common courtesy to discuss this with her privately, not play judge, jury, and executioner.

★< [https://ad-science.org/2021/10/21/notes-from-a-molecular-biologist/?like\\_comment=57&\\_wpnonce=c91be175f2](https://ad-science.org/2021/10/21/notes-from-a-molecular-biologist/?like_comment=57&_wpnonce=c91be175f2)>

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DD

**October 26, 2021 at 8:39 am < <https://ad-science.org/2021/10/21/notes-from-a-molecular-biologist/#comment-60>>**

Bik is a part of the shorter cartel behind the CP despite her denials. and given that she is also a narcissist, she will never admit that she's wrong.

★< [https://ad-science.org/2021/10/21/notes-from-a-molecular-biologist/?like\\_comment=60&\\_wpnonce=656ecb5bf7](https://ad-science.org/2021/10/21/notes-from-a-molecular-biologist/?like_comment=60&_wpnonce=656ecb5bf7)>

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Retired MD, PhD

**October 26, 2021 at 9:01 am < <https://ad-science.org/2021/10/21/notes-from-a-molecular-biologist/#comment-61>>**

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Commodore64\_

**October 23, 2021 at 12:56 am <<https://ad-science.org/2021/10/21/notes-from-a-molecular-biologist/#comment-58>>**

Well written.

At the end of the day stuff from years ago has no real relevance to the current data we have on hand.

Does placebo effect still work for 12 long months with AD patients? If no, the drug works. Can AD patients magically start fake getting better for 12 months? 🚨 Yeah didn't think so. The drug works!

Can placebo modify biomarkers in any meaningful way? If no, the drug works.

A safe drug that works. There's so much FUD trying to rob retail of their precious golden tickets. I am Not selling. I can see through the lies, misdirections, and irrelevant arguments of the shorts and their "helpful" idiots on Twitter. SAVA is the real deal!

★<[https://ad-science.org/2021/10/21/notes-from-a-molecular-biologist/?like\\_comment=58&\\_wpnonce=c1afdf54dd](https://ad-science.org/2021/10/21/notes-from-a-molecular-biologist/?like_comment=58&_wpnonce=c1afdf54dd)>

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